

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US05/12218

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC(7) : C07D 491/02 US CL : 548/453 According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) U.S. : 548/453 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2003/0157695 A1 (FENICAL et al) 21 August 2003 (21.08.2003)	1-24
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.		
* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search 26 October 2005 (26.10.2005)		Date of mailing of the international search report 15 NOV 2005
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-8300		Authorized officer Robert Shiao Telephone No. (571) 272-1600

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

REC'D 17 NOV 2005

PCT WIPO PCT

To:  
ERNEST V. LINEK  
28 STATE STREET - 28TH FLOOR  
BOSTON, MA 02109

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing (day/month/year) <b>15 NOV 2005</b>		
<b>FOR FURTHER ACTION</b> See paragraph 2 below		
Applicant's or agent's file reference  004979-00048		
International application No.  PCT/US05/12218	International filing date (day/month/year)  11 April 2005 (11.04.2005)	Priority date (day/month/year)  09 April 2004 (09.04.2004)
International Patent Classification (IPC) or both national classification and IPC  IPC(7): C07D 491/02 and US Cl.: 548/453		
Applicant  PRESEDENT AND FELLOWS OF HARVARD COLLEGE		

1. This opinion contains indications relating to the following items:

- |                                     |              |  |
|-------------------------------------|--------------|--|
| <input checked="" type="checkbox"/> | Box No. I    | Basis of the opinion   |
| <input type="checkbox"/>            | Box No. II   | Priority   |
| <input type="checkbox"/>            | Box No. III  | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability   |
| <input type="checkbox"/>            | Box No. IV   | Lack of unity of invention   |
| <input checked="" type="checkbox"/> | Box No. V    | Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/>            | Box No. VI   | Certain documents cited  |
| <input type="checkbox"/>            | Box No. VII  | Certain defects in the international application   |
| <input type="checkbox"/>            | Box No. VIII | Certain observations on the international application  |

### 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-8300	Date of completion of this opinion  26 October 2005 (26.10.2005)	Authorized officer Robert Shiao Telephone No. (571) 272-1600
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WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

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Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of:

- ☒ the international application in the language in which it was filed  
☐ a translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

- ☐ a sequence listing  
☐ table(s) related to the sequence listing

b. format of material

- ☐ on paper  
☐ in electronic form

c. time of filing/furnishing

- ☐ contained in the international application as filed.  
☐ filed together with the international application in electronic form.  
☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE  
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**Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims <u>1-24</u>	YES
	Claims <u>NONE</u>	NO
Inventive step (IS)	Claims <u>1-24</u>	YES
	Claims <u>NONE</u>	NO
Industrial applicability (IA)	Claims <u>1-24</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and explanations:

Claims 1-24 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest what the instant compounds are. This invention relates to simple stereocontrolled synthesis of salinosporamide A. The closest prior art is Fenical et al. US 2003/0157695, discloses marine actinomycete taxon for drug and fermentation product discovery. The difference between prior art and instant claims is that the instant processes of making and their intermediates are not found in Fenical et al. Suggestion for modification of above reference to obtain the instant claimed processes and their intermediates, has not been found.

Claims 1-24 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.